Brain Tissue: Analysis of Mechanical Properties

In accordance with requirements

in order to graduate with Distinction from

Department of Mechanical Engineering at

The Ohio State University

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Abstract

The overall research was conducted to better understand the mechanical behavior of brain tissue. My portion of the research specifically examined the difference of mechanical properties for stored versus fresh brain tissue. The goal was to determine a way to compare data from stored brain tissue to fresh brain tissue and to establish a correlation between the data. It was important to better understand the mechanical properties of brain tissue because, provided a better understanding, new strides could be taken to better understand the reaction of the brain with possible biocompatible implants. Fresh brain tissue was provided from a species of monkey (Macaque), which was used for a majority of the experiments and was compared to stored human brain tissue. Tests were conducted on the brain tissue using varied strains and strain rates. For a variety of these tests hyperelastic/viscoelastic models were constructed to mimic the tissue response to strains. Results showed that stored tissue was stiffer when compared with fresh tissue, but have similarly shape stress-strain curves. Results also suggested that with a larger sample data, there could possibly be a correlation drawn between stored and fresh tissue samples. These results have important implications because fresh brain tissue is difficult to attain and work with.

Acknowledgements

The PhD student overseeing the project was Sarah Bentil, who helped with each portion of the project from the experimental design through the conclusions reached. I would like to thank Professor Rebecca Dupaix for donating her time and effort, as well as her research lab in order to allow Sarah and me to conduct experiments. Professor Dupaix's other research students, Kamakshi Singh, and Srinath Sistla helped to introduce stress/strain equipment. Other thanks goes out to Mike Boehm and Dr. Heather Powell for access and training on additional equipment required to sufficiently examine the brain tissue. Lastly, many thanks go to Dr. Sarkar and his lab assistants for providing fresh brain tissue.

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I. Introduction

The purpose of this research was to observe and gain understanding of the stress-strain behavior of stored brain tissue compared to fresh brain tissue. The main objective was to determine possible correlations between the stored and fresh tissues. This was seen as an important topic because if a correlation could be drawn then future research could test strictly using stored tissue and determine the reaction of in-vivo tissue, allowing research to be less dependent on the need to use fresh tissue. First it was desired to standardize the test procedure to ensure that upon the reception of brain tissue we would not waste any time or tissue. Once that was completed we moved to testing stored tissue, which provided promising results, so it was decided to move forward with testing of fresh tissue. At this point it was discovered our test mechanism was inefficient for such a soft material so new test mechanisms were determined and used. Once the tests were completed, hyperelastic/viscoelastic models were derived for several tests, and their constants were analyzed to determine if any trends were present. Few trends were found but the future work in this field seems quite promising.

II. BACKGROUND

Neurons are responsible for the information process within the brain, but neurons compose fewer than 25% of the cells in the brain [1]. When a neural path of the CNS has been damaged, the brain can no longer transmit information via neurons along that path. In order to compensate, the brain attempts to extend neural endings around the damaged area and periodically the brain cannot successfully do so [1]. In these cases, there are various ramifications such as loss of motor skills or speech [1]. Neural implants are one possible way to continue transmitting information despite the presence of damaged neurons in the CNS. Thus, they are useful in many medical applications, including the treatment of hearing loss, visual restoration, and the recording of epileptic seizures [1].

Various issues are caused by neural implants but we plan to focus on the biocompatibility between the implant and the brain tissue. The implants currently consist of metal electrodes (ie Au, Ti, Pt, IrOx), supported on polymer substrates (ie polyimide, polyurethane) [2]. However, metals and polymers differ in mechanical properties from the brain tissue. As a result, the brain recognizes the implant as a foreign body and begins to mount an attack over time, rendering the implant ineffective.

When the brain attempts to reject the implant, cells begin to build up around the implant moving it farther and farther away from the neuron soma [1]. This reduces the effectiveness of the implant since it depends on the proximity to the neuron soma and its cellular processes.

The purpose of this research was originally to find a more effective/biocompatible material to coat the neural implant, but instead evolved into testing brain tissue in the attempt to better understand the tissue's response to strain. There has been limited research in the field of soft human tissues, including the brain, therefore making it difficult to design a device to improve mechanical compatibility, without knowing how the soft tissue reacts to mechanical deformation. With better understanding of the tissue's response and the development of a new material to mimic the brain, an implant could possibly be placed in the brain without a reaction from the body. The dilemma remains that the brain is soft tissue, therefore it does not have a linear stress-strain curve [3].

An experimental procedure needed to be developed to test material properties of brain tissue. According to Miller [3] the stress-strain curves of brain tissue are concave upward, lacking a straight portion which prohibits the determination of an elastic modulus. In the past, the tissue response had been observed to be rate dependent. When the stresses were applied to the tissue at high rates the response was up to six times higher when compared to the lower compression rates [3]. From the mathematical modeling a better understanding can be developed in regard to the brain tissues response to the insertion of a neural implant. In Miller's work, there was discussion surrounding the strain rates at which the compression tests were conducted: Fast-500 mm/min, Medium-5mm/min, and Slow-0.005 mm/min. In his work he was able to test at all of these strain rates. We chose to used the Medium rate because it was approximately the speed at which neurological implants are put in, therefore used in the analysis of the tissue. The other two rates were chosen because they are two orders of magnitude greater

than the surgical procedure, therefore providing data from completely varied strain rates [3].

Miller examined the ability to model the soft tissue in a finite element model, in an attempt to mimic surgical procedures, and did so using ABAQUS [4]. He chose to model the tissue as what he referred to as a "simple, linear viscoelastic model" of tissue deformation. The model potentially could account for observed non-linearity in the stress-strain relationship, taking into account the dependence on the strain rate. In order to generate constants for hyperelastic and linear viscoelastic model, he used the polynomial strain energy function for a hyperelastic, linear viscoelastic medium written as seen in Equation (1).

$$W = \int_0^t \left\{ \sum_{i+j=1}^{N} \left[C_{ij0}\left(1 - \sum_{k=1}^{n} g_k\left(1 - e^{-t-\tau/\tau_k}\right)\right)\right] \times \frac{d}{d\tau}\left[(J_1 - 3)^i (J_2 - 3)^j\right] \right\} d\tau \qquad (1)$$

Within Equation (1) τ_k are characteristic times, g_k are relaxation coefficients, N is the order of polynomial in strain invariant, J_k are strain invariants, and C_{ij0} describes the instantaneous elasticity; all of which are described in greater detail within Miller [4]. From Equation (1) Miller conducted a regression and found the fit of least squares to his data for a variety of rate test data. After several iterations he determined the coefficients he wanted to use in his modeling within ABAQUS, which can be seen in Table 1. These constants were later used in our attempt to model our data within ANSYS.

Instantaneous response	Characteristic time $t_1 = 0.5$ (s)	Characteristic time $t_2 = 50$ (s)
$C_{100} = C_{010} = 263$ (Pa) $C_{200} = C_{020} = 491$ (Pa) $C_{110} = 0$	$g_1 = 0.450$	$g_2 = 0.365$

Table 1: Constants from Miller 1999

III. EXPERIMENTAL PROCESS

The experimental process was quite basic, revolving around unconfined compression tests. The tests involved had two plates that would compress the brain tissue to a previously defined displacement at a pre-determined rate. It allowed the test to be monitored and changed at our discretion with very simple variables dictating the test. Aside from performing unconfined compression another test was set up centering on the use of an indenter, with the same set of parameters. The indenter could be a variety of shapes, but the relationship between the indentation results and the actual mechanical properties, so these tests were strictly used for comparison purposes. Through this process several soft tissues were analyzed and dictated the course of the overall research.

The stress v. strain relationship as well as the relaxation response of soft tissue was analyzed using three separate mechanisms: Instron, Rheological Solid Analyzer (RSA) and the TestResources' Servo-compression Machine. Each of these test mechanisms had to be able to perform a sequence of three strain functions: loading, hold and release of strain. From the data collected the stress v. strain curves were generated and compared.

III.I Preliminary Experiments

Initially the Instron was used to collect data. Originally it was chosen because it was located in Dr. Dupaix's Laboratory, therefore it was readily available. It had the capability to conduct both unconfined compression tests as well as indentation tests,

where both sets of data were desired for comparison purposes. The Instron was also able to have an input of compression followed by a hold finishing with the removal of the strain. This was very desirable, seeing as we wanted to examine both the tissue's stress-strain response and its stress relaxation response. It had the capability of conducting tests using a 50 kN load cell as well as a 500 N load cell.

Before conducting experiments on fresh brain tissue it was important to better understand our test equipment, and the overall reaction of soft tissue. We wanted to analyze a form of soft tissue that would allow us to troubleshoot the overall experiment, without wasting valuable fresh tissue samples. We also wanted to verify the specifics of the test procedure such as the test set up, precautionary measures, sequence of events and to verify whether our test apparatus was sufficient.

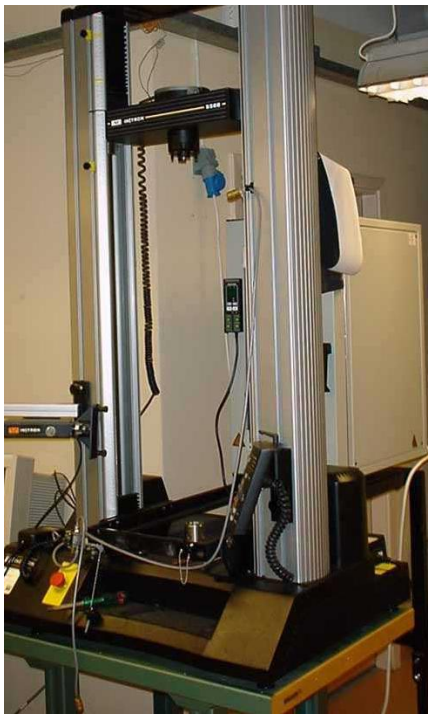

Figure 1: Instron

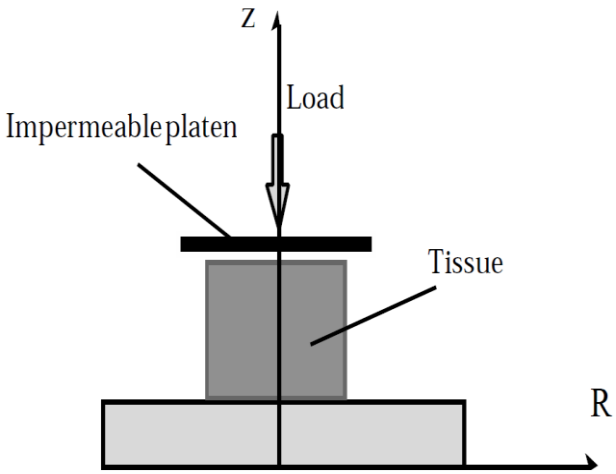

Figure 2: Experimental Layout

The experiments commenced with the tests being conducted using chicken breast purchased from the supermarket. Even though the chicken breasts' properties were different from brain tissue, it was a form of soft tissue able to be used to simulate the soft tissue response. Chicken breast was chosen because it was readily available and inexpensive. The chicken breast was tested using an unconfined compression test, conducted on an Instron, as seen in Figure 1. Our initial test set up was based off of Figure 2, which displays a schematic of a soft tissue test taken directly from the work conducted by Miller [3]. During testing, the tissue was placed between two small sheets of Teflon in an attempt to limit the friction acting on the tissue. A load cell of 50 kN was used for the unconfined compression, but after conducting tests with different parameters we also wanted to analyze the response of using an indenter. The indenter required a smaller load cell (500N), which would also supply more accurate readings. When the indenter test was conducted, there was a sheet of Teflon placed on the base of the tissue, but the top of the tissue was directly contacted by the indenter.

In order to ensure the tissue samples were consistent in size a coring tool was developed. It was used on each test conducted, including stored and fresh brain tissue samples. It generated cylindrical samples that were approximately 28.5 mm in diameter. The cored pieces of tissue were then cut such that each sample was measuring approximately 10-15mm in height. There was concern over whether or not the cutting

instrument actually damaged the tissue, but it was the best and most consistent way of cutting the tissue.

The Instron required that the input be entered into the computer as time steps. The issue was that we were dealing with dynamically changing strains; meaning we needed to enter as many steps as possible in order to generate an input that mimicked our desired control of the overall strain and strain rate. In order to simplify the calculations an excel sheet was created that determined the time steps from the rate and overall displacement (as seen in Appendix 1).

The response of the chicken breast can be seen in Figures 2 and 3. The input was shown using a strain v. time curve, which shows the compression, then holding period, leading the removal of strain. The chicken breast test was conducted for the sole reason of determining whether our test setup was adequate, and from the results seen below, we concluded our procedure was sufficient. Due to the success of the chicken breast test, it was decided to move on with the experiments to using human brain tissue that had been stored in Paraformaldehyde.

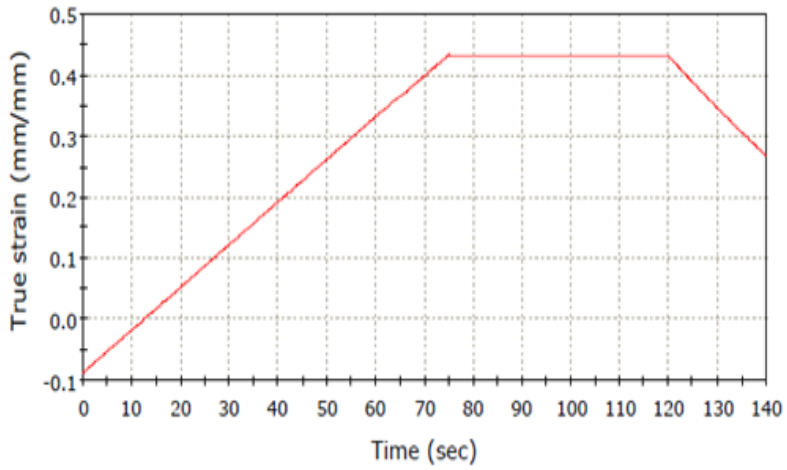

Figure 3: Strain v. Time – Instron Input

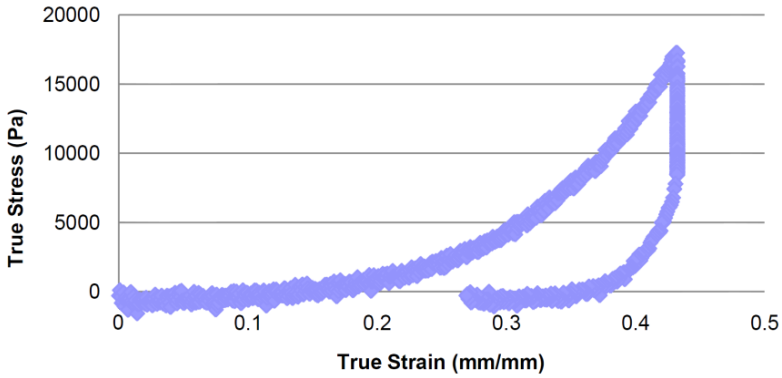

Figure 4: Stress v. Strain – Instron Output for Chicken Breast

We were able to attain brain tissue stored in Paraformaldehyde from Dr. Bolte. The stored brain tissue was from cadavers that had been used for other forms of tests, and the two brains had yet to be tested or handled. Both brains had been stored in the Paraformaldehyde for 6-12 months. Paraformaldehyde is always used to preserve organs, because it binds the proteins within the tissue, therefore limiting degradation. Its effect on the mechanical properties of the brain tissue, compared to fresh tissue, was unknown; therefore it seemed like a logical step toward working with fresh tissue.

There were an array of unconfined compression tests conducted on the Instron, but Figure 4 shows the tests that were conducted using a strain rate of 5 mm/min. A strain rate of 5mm/min was used because as explained in Miller [3], neurological surgeries take place at approximately that strain rate. It was encouraging to see the presence of relaxation and hysteresis, which was expected. The overall strain seems slightly different, but that can be attributed to the varying heights of the initial sample. In Figure 4 the set of data labeled "~25% Strain Sample D" was not consistent with the other three tests present. In terms of stress it only reaches about half of the other tests, even though each of the tests experienced the same displacement and rate.

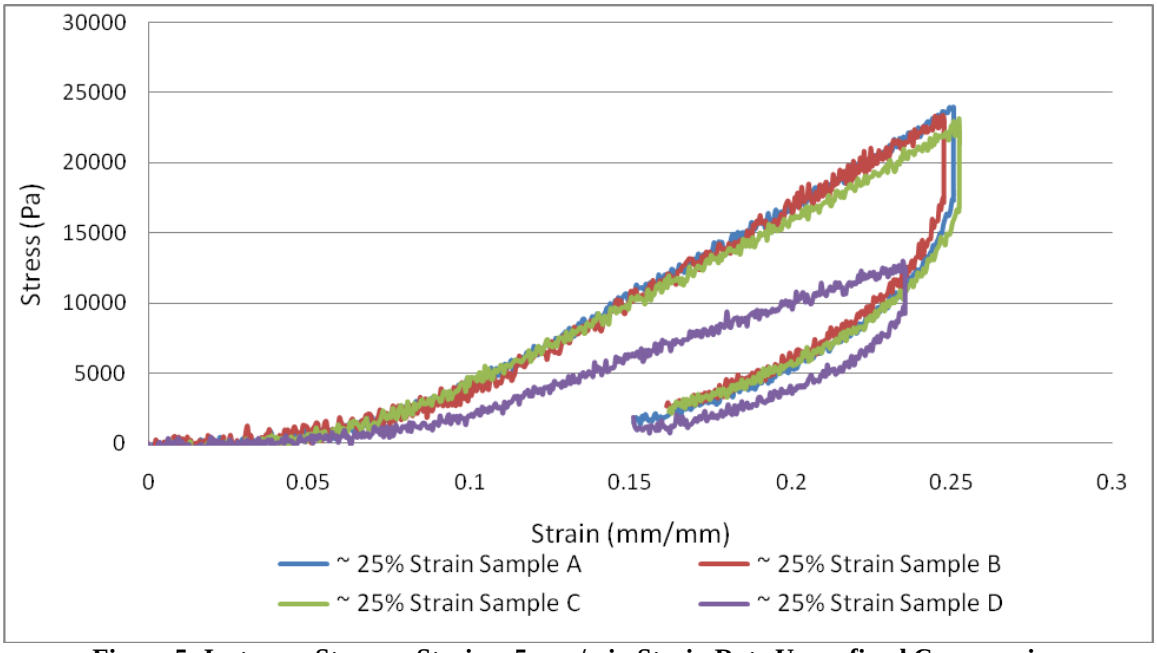

Figure 5: Instron – Stress v. Strain – 5 mm/min Strain Rate Unconfined Compression

Once the unconfined compression tests were finished, we desired to see how the data compared to indenter tests that were also possibly conducted. The indenter used had

a diameter of 0.5 cm, and was spherical at the tip. A set of sample data can be seen in Figure 6, and for comparison purposes both Figure 5 and Figure 6 tests have a strain rate of 5 mm/min.

The indenter data in Figure 6 only consists of two sets of data. These two tests were chosen for comparison because the two samples were identical in height, and had identical inputs, which would have hopefully produced data that was consistent. Notice that the x and y axis of Figure 6 was in terms of Load v. Displacement. The reason for this difference from the previous tests was because the Indenter was used to conduct this test. The indenter could not generate data in terms of Stress v. Strain because the relationship between the contact point and the remainder of the tissue was not yet fully understood. Even though the x and y labels are different, the shapes could be easily compared to the previous tests. Each indenter test data set was examined using the Load v. Displacement. The results produced fairly similar curves. The general shape was the same, but the maximum load reached was not as high in the 2^{nd} sample. These problems are most likely due to the inability to conduct identical tests, in terms of when contact was made between the mechanism and the sample, as well as inaccurately measured heights.

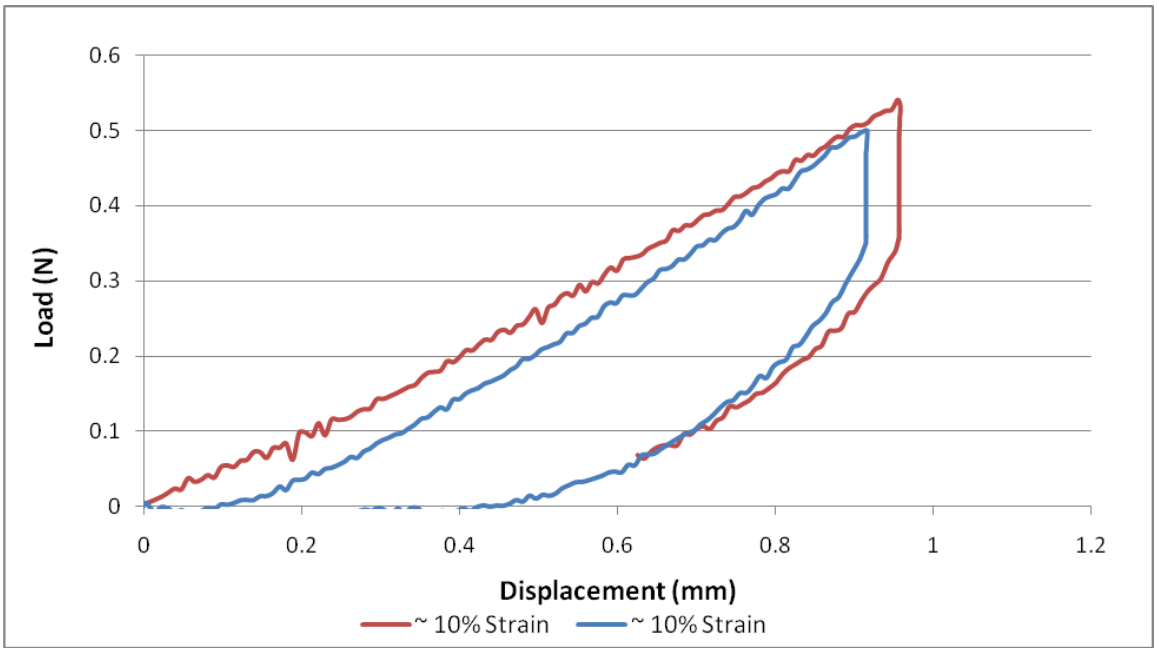

Figure 6: Instron Indenter – Stored Human Tissue – 5 mm/min Compression Rate – 10 mm sample

Once the stored tissue was analyzed it was determined, that the test procedure had been standardized, and it was time to move onto fresh tissue. Once the fresh tissue was tested we could then move forward with data analysis.

III.II Fresh Tissue Experiments

Fresh brain tissue was provided by Dr. Sarkar's Lab. The tissue was available because one of Dr. Sarkar's cohorts was conducting tests on the Macaque Monkeys and once the tests were completed, the monkeys were to be sacrificed, and the tissue was available. Prior to conducting any tests it was brought to our attention the dangers of working with Macaque Monkeys. Alarming percentages (approximately 70%) of Macaque Monkeys are infected worldwide with Herpes B, which if transmitted to

humans could potentially be fatal. The symptoms resemble meningitis and could potentially result in death, if not treated properly. Due to the risks associated with working with these monkeys more precautions were taken and practiced. The member of the research team who would be handling the tissue would be required to wear two layers of gloves, a smock, eye protection, mouth protection. These precautions made it difficult to perform the tests as compared to normal conditions. In addition, any cutting of the tissue was to be conducted on a specially provided absorbent sheet to ensure that none of the fluids would be transmitted. Once all testing was completed anything that could have potentially been brought in contact with the tissue would have to soak in bleach water, and then be washed with soap and water to ensure that each instrument was not carrying potentially dangerous virus. We practiced this process several times using the other soft tissues previously mentioned, to ensure that we would be prepared once the fresh tissue was provided.

It was important to test the brain tissue as soon as possible upon removal, to ensure that the tissue samples were as similar to in-vivo brain tissue. During our first attempt we were able to conduct tests only a few hours after removal. We had planned to conduct indenter tests because the load cell for the indenter was 500 N compared to the unconfined compression load cell which was 50 kN and the smaller load cell could produce more accurate data, as well as eliminating some noise.

The original test set up was to test the brain tissue at previously determined times to establish how the material properties changed over time in different mediums. The

problem was that once we initiated the tests we discovered that the Instron could not properly detect the stresses within the tissue. The tissue was too soft in comparison to the previous soft tissue used. The readings from the Instron were cluttered with noise as seen in Figure 7 rendering the data useless.

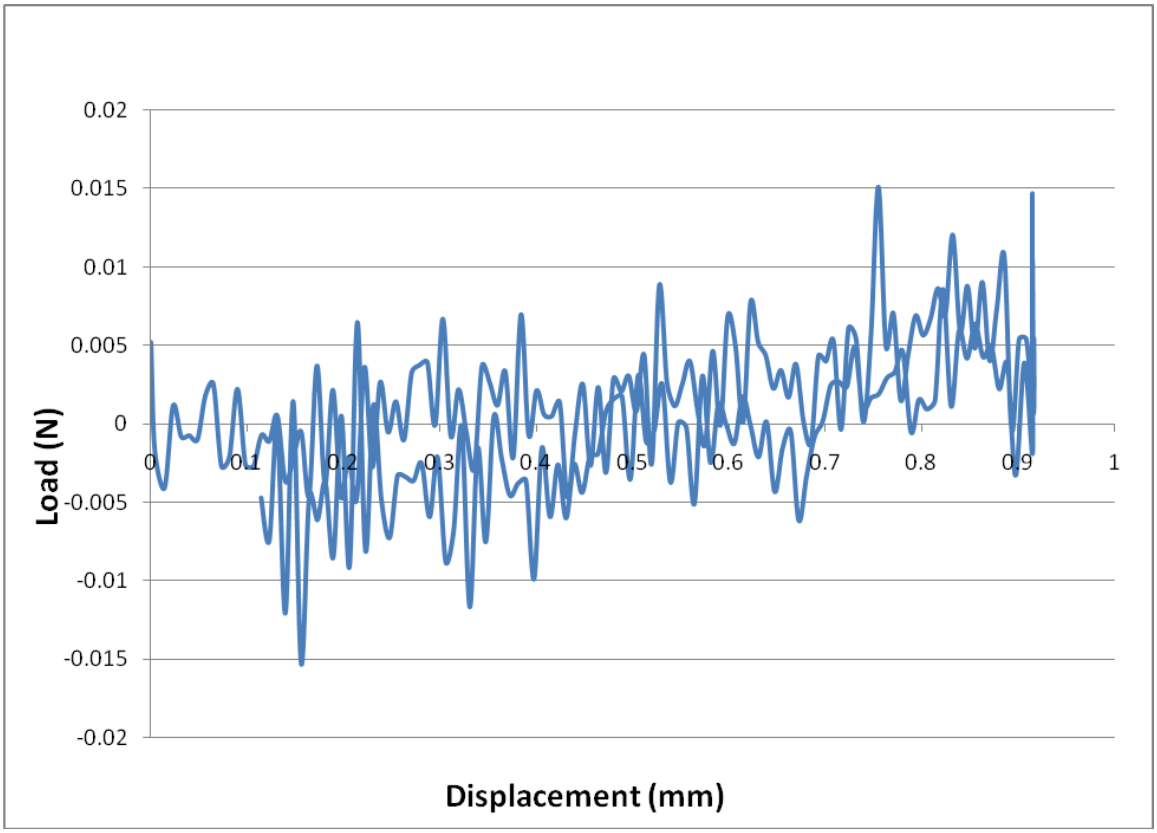

Figure 7: Instron Indenter – Fresh Macaque Tissue - 5 mm/min Compression Rate – 10 mm sample

A new testing mechanism needed to be found before any more tests could be performed on fresh tissue. Luckily enough there were two possible alternatives available: The Rheological Solids Analyzer (RSA) and the Servo Compression Machine by TestResources.

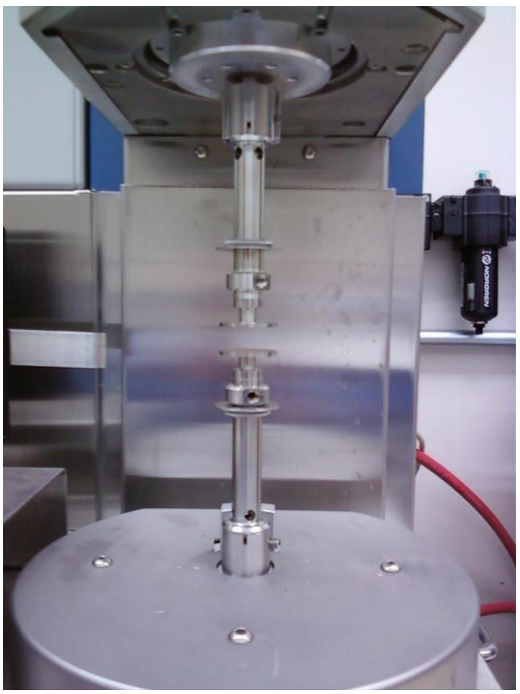

Figure 8: Rhelogical Solid Analyzer

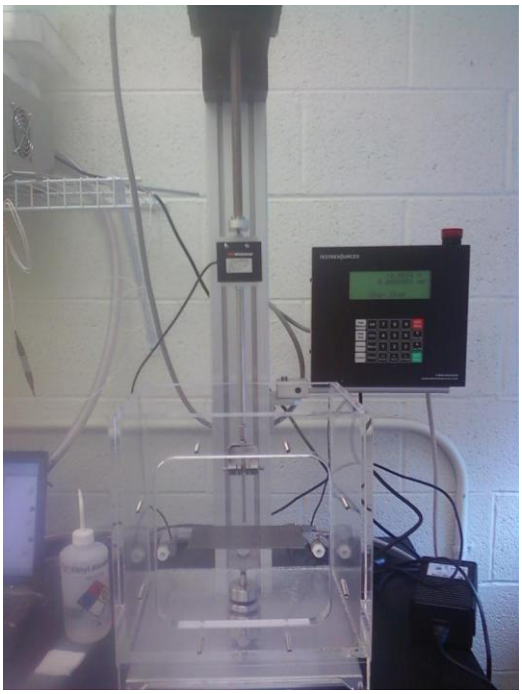

Figure 9: TestResources Machine

In order to use the new equipment we needed to be trained using each apparatus, to make sure that we were still holding fast to our original test parameters. We were first trained on the RSA. The other alternative to the Instron was the Rheological Solid Analyzer (RSA). This test mechanism differed from the Instron because it was only capable of conducting unconfined compression tests, although it was able to have an input of a compression followed by a hold finishing with the removal of the strain. The load cell of the RSA was 20 N which was much lower than the Instron, which had load cells of 50 kN and 500 N. The smaller load cell would eliminate noise collected by the mechanism, providing much more accurate data. The RSA was not located in a readily available location, because it was located in the Rheology Lab within Kofolt Lab. The

RSA was the mechanism whose data was used for a majority of the analysis, but that was because the only valuable data collected from fresh tissue was collected using the RSA.

We were sufficiently able to control the strain in the equipment, allowing for a loading/hold/unloading input, adhering to our original test parameters. The limitation of using the RSA was that the only test that could be performed was the unconfined compression test, because it had designated plates that fit into the overall setup. This limited the data that could possibly be collected from the mechanism. Even though there were limitations, we chose to conduct unconfined compression tests using stored tissue initially, as seen in Figures 10 and 11.

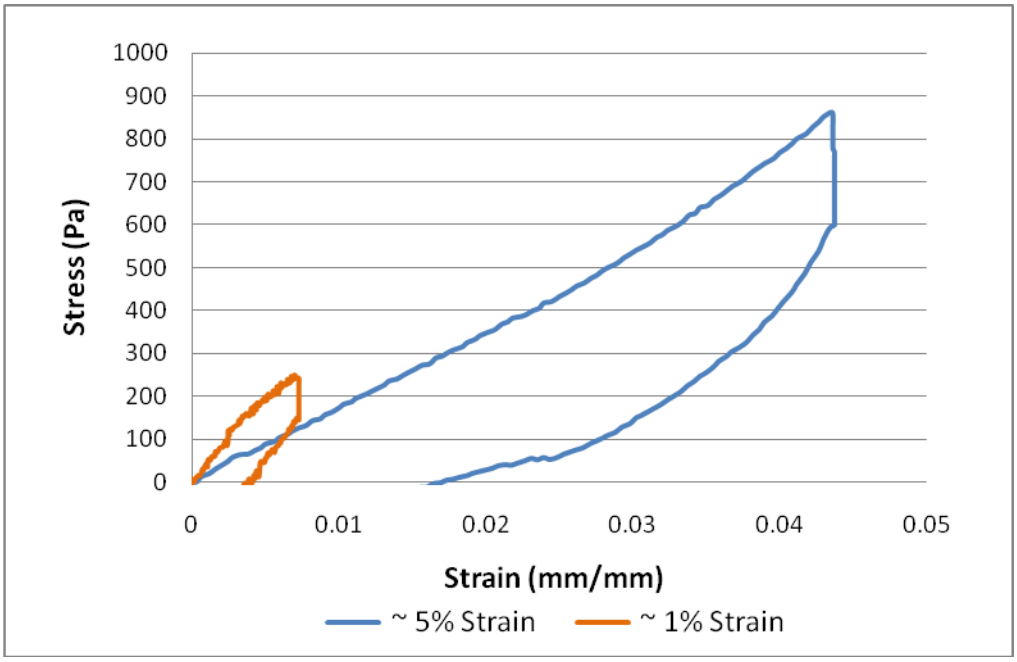

Figure 10: RSA – Low Strains at Strain rate of 5 mm/min

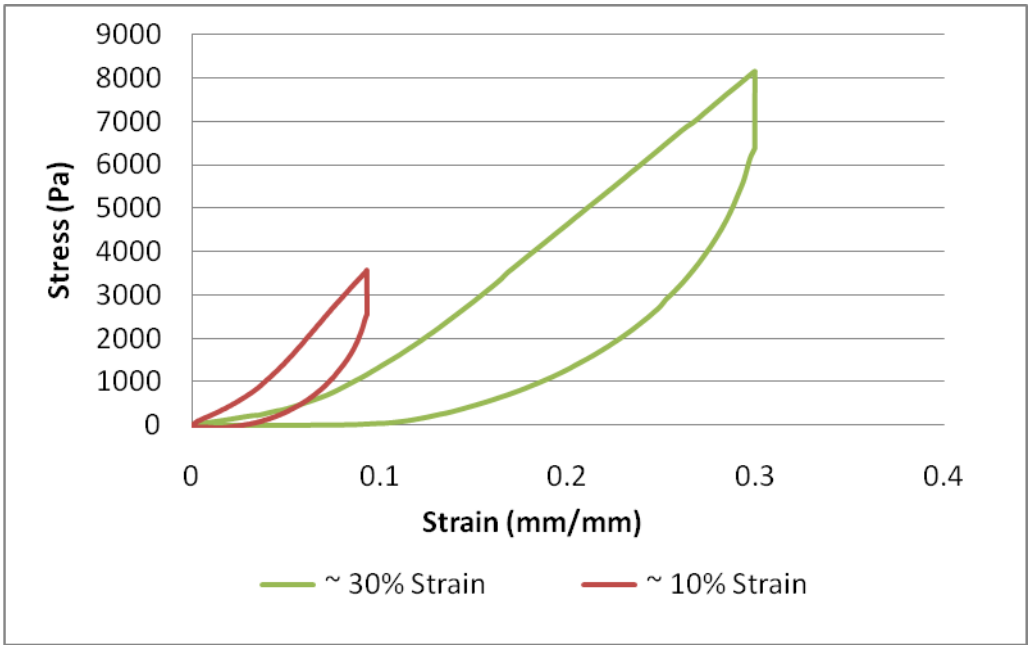

Figure 11: RSA – High Strains at Strain rate of 5 mm/min

Within both Figures 10 and 11, there are some noticeable trends regarding the stress-strain relationship upon the increase in strain rate. In both figures as the strain was increased the stress. Also, the relaxation of the tissue during the hold period extends as the strain increases. These relationships will be examined more when the models generated from these plots are discussed.

Looking strictly at the "smoothness", which corresponds to the of the data in Figures 9 and 10, compared to Figures 4 and 5 from the Instron, that the RSA would be able to measure much lower stresses, in comparison and hopefully the fresh tissue. At this point it was time to move forward and test fresh Macaque Brain tissue.

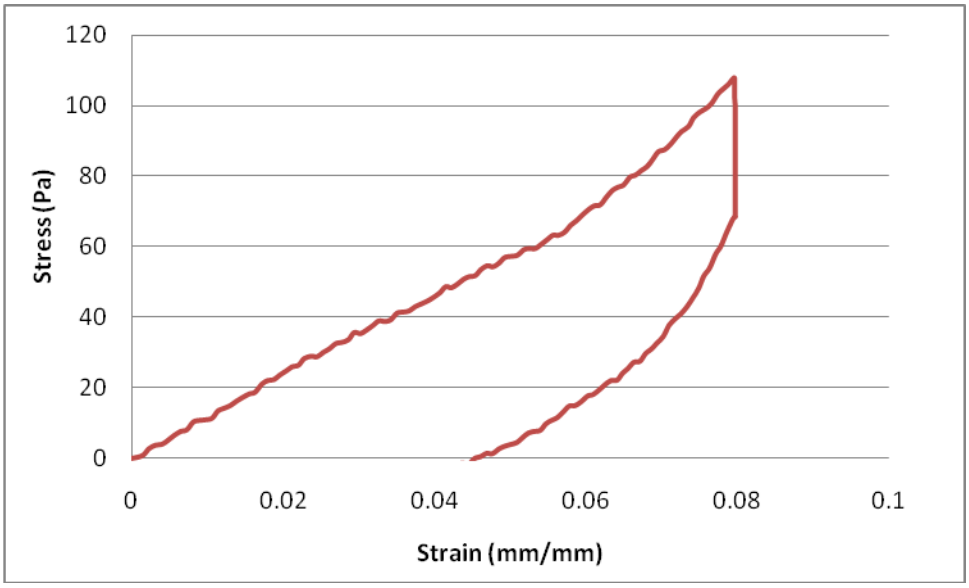

Figure 12: RSA – Stored Human Tissue – 7.9% Strain at a Strain Rate of 5 mm/min

The Fresh Tissue response followed the same general shape of the stress v. strain curve of the human brain. In Figure 12, the same strain rate was used as in Figures 5, 6, 7, 10 and 11, in order to maintain consistency. The response seen in Figure 12 was encouraging to our overall goal because the stress-strain response has nearly the same concave shape as the stored brain tissue seen in Figures 10 and 11. The stesses attained by this test, when comparing to the stored tissue test at approximately 10% strain present in Figure 11, it was easy to recognize that the stored tissue produced much higher stresses. Once this test was completed we decided to conduct a test with a high strain rate and high strain, in order to use it to contrast the already collected data. Sadly, this descision produced an interesting set of data, but a repeat of the test parameters seen in Figure 12 may have been a wiser choice, in order to verify our data.

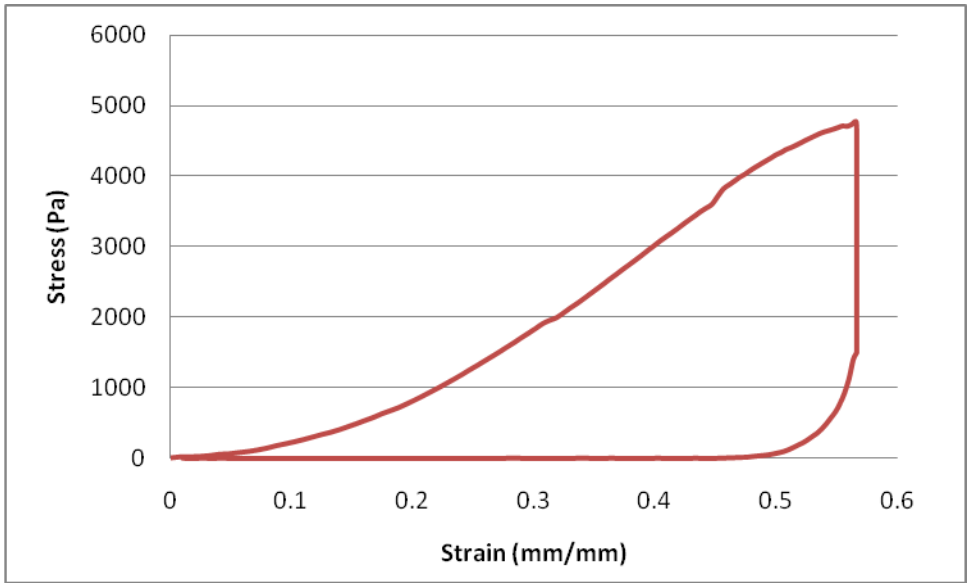

Figure 13: RSA – Stored Human Brain – 56.7% Strain at a Strain Rate of 40 mm/min

The data of the extreme strain and strain rate can be seen in Figure 13 and the shape of the response differs from previous tests, but that was expected. The response in Figure 13 had a convex beginning similar to Figure 12, but as the test approaches the hold portion the stress v. strain curve begins to bend down, which was not seen in any of the other tests conducted up to this point. The tissue response in Figure 13 was much stiffer when compared to the tissue in Figure 12. The slope of the compression portion of the test within Figure 12 was approximately 1400 Pa compared to the slope taken from the linear middle section of Figure 13 which was approximately 11000 Pa. This difference was huge, nearly an entire order of magnitude higher, using the same tissue, proving the importance of being consistent regarding the strain rate, when comparing tests. As stated previously the RSA machine was only able to conduct unconfined compression tests, therefore we still desired the ability to test using an indenter.

After collecting data from the RSA, another apparatus was introduced, the Servo-Compression Machine from TestResources. This test setup was very comparable to the Instron, as it had the capability of conducting both unconfined compression tests as well as indentation tests, while also being able to have an input of a compression followed by a hold finishing with the removal of the strain. The load cell of the TestResources mechanism was 10 N which would provide even more accurate data then both other test mechanisms previously discussed. This seemed like a promising route but one problem was that it was located in Dr. Heather Powell's Laboratory in Fontana Labs.

The TestResources machine could potentially allow for a better comparison between the two forms of tissue, fresh and stored, the only issue was that we have been waiting for fresh tissue samples, but there were a variety of tests conducted using its indenter on stored tissue. An example can be seen in Figure 14, were similar to that of the test from the Instron and the RSA in order to provide how the data compares and could potentially be quite useful if provided fresh tissue.

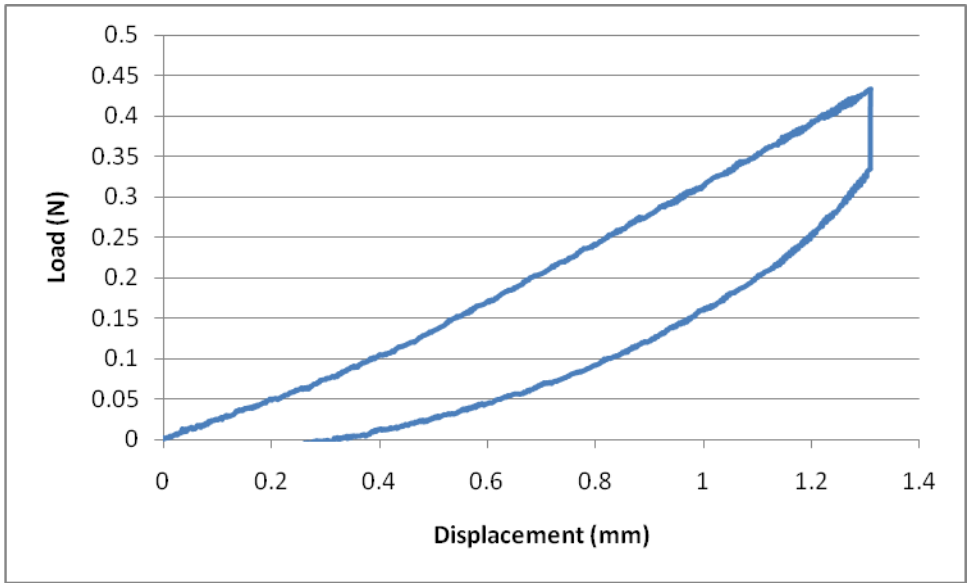

Figure 14: TestResources – Stored Human Tissue – 5 mm/min Compression Rate – 13 mm sample

Once all the data was collected it was important to find the best set of data that could be compare fresh and stored tissue. The most useful set of data was collected using the RSA, because not only was there data collected from the stored human brain, but also semi-fresh tissue (only days old). Therefore, the RSA provided the best data to derive solid models from in an attempt to find a correlation between stored and fresh tissue stress-strain behavior.

IV. Solid Modeling

In order to better understand the data collected it was imperative to model the brain tissue in a form of software. It was decided to analyze the data using ANSYS, because of our previous experience in it. The tissue was modeled as a solid cylinder with a radius of .01425 which equated to the 28.5 mm diameter of the cut samples. The height

of the model varied with each of the tests conducted. The bottom face of the cylinder was limited to have zero displacement in the Z-direction. A node on the bottom face was selected indiscriminately, and given zero degrees of freedom, in order to keep the model from moving in the x and y directions inappropriately. The nodes located on the top face were then coupled together. When nodes are coupled, they are all controlled by the lowest numbered node in the coupling. The material properties were added at this time before the test was conducted, but were varied for each test, and will be further discussed later. The desired displacement was then placed on the controlling node, and the simulation was run. After running the simulation, the force required to displace the sample was obtained as the reaction force on the controlling node. The controlling node had all of the reactionary forces on it because all the nodes on the face were coupled together, allowing to compare the time/force/displacement from the model to the actual data collected.

It was decided after reading Miller [4] that the best way to model the tissue was as a viscoelastic/hyperelastic material. In Miller [4] they were able to apply both material properties, viscoelasticity and hyperelasticity to their model, but they used ABAQUS rather than ANSYS. The constants they applied can be seen in Table 1, within the background.

The hyperelastic model equation in accordance with ANSYS Help Menu was actually the strain energy density function that can be seen in Equation (2).

$$\bar{W} = \sum_{i+j=1}^{n} C_{ij}\ (\bar{I}_1 - 3)^i\ (\bar{I}_2 - 3)^j + \sum_{i=1}^{n} \frac{\kappa_i}{2}(J-1)^{2i} \quad (2)$$

W = strain energy potential
I_1 = first deviatoric strain invariant
I_2 = second deviatoric strain invariant
J = determinant of the elastic deformation gradient ***F***
C_{ij} = material constants

To input viscoelastic effects we used the Prony Model for shear response, which predicts a viscoelastic response provided times and shear moduli at those times. It was suspected that the hyperelastic constants will have a greater affect on the loading response and the viscoelastic constants will have a greater affect on the holding portion of the test where the tissue was maintained at a constant strain.

When Miller [4] was examining the brain tissue, he only examined the loading portion of the stress, from 0 to -0.25 true strain, where we were hoping to examine the loading, a maintained strain and then the unloading of the tissue. Therefore, our models will look very different, and examine different portions of the stress-strain curve, but the constants seen in Table 1 would be used as a starting point of our iterations to determine the constants that best represent our data.

In order to create a base-line it was decided to compare unconfined compression tests, where each test was performed at 5 mm/min, with strains ranging from 1% to 30%, for Human tissue stored in Paraformaldehyde. The hope was to be able to compare the

models from the stored human tissue to the fresh monkey tissue, which was able to be done at the target test parameters of 5 mm/min and 10% strain.

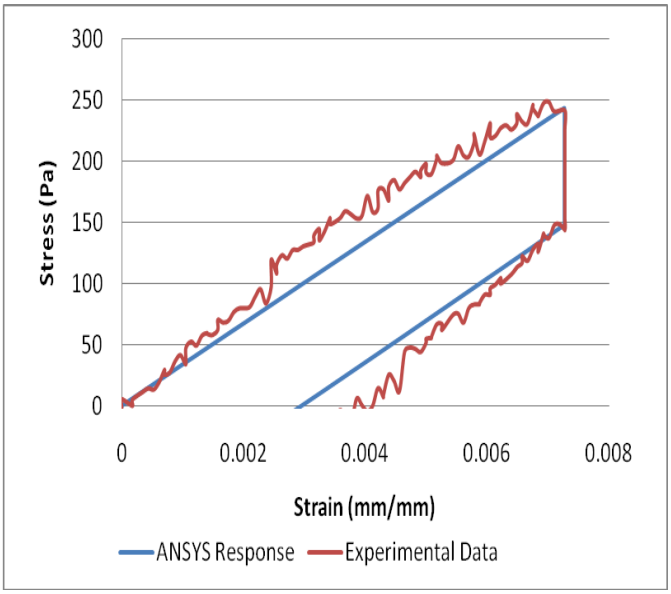

Figure 15: RSA – Stress v. Strain – Stored Human Tissue 0.70% Strain with ANSYS Model

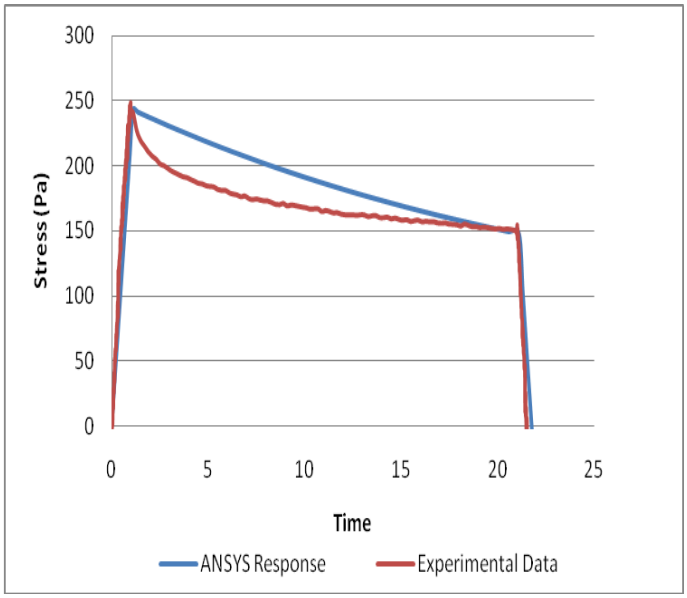

Figure 16: RSA – Stress v. Time – Stored Human Tissue 0.70% Strain with ANSYS Model

Figures 15 and 16 represent the lowest strains applied to the stored human tissue samples. Notice that the compression portion of the Experimental Data from Figure 15 has a convex shape, which was a different response when compared to the test conducted on the Instron and TestResources machines. This was most likely due to using such a low strain rate, and the noise that came with it. The model used could only attain concave formations so the fit in Figure 15 was the best possible. After performing the iterations in order to generate the Stress v. Strain curves, it was determined that the Stress v. Time curve would provide a better representation of the viscoelastic performance, as seen in Figure 16. During the compression and release-of-strain portion the Experimental Data seems quite linear, but the holding portion does not. The hold was convex with a very

steap initial sloap, which leveled out quickly. The model does not accurately depict the response during the hold, but acurately predicts the beginning and the end points.

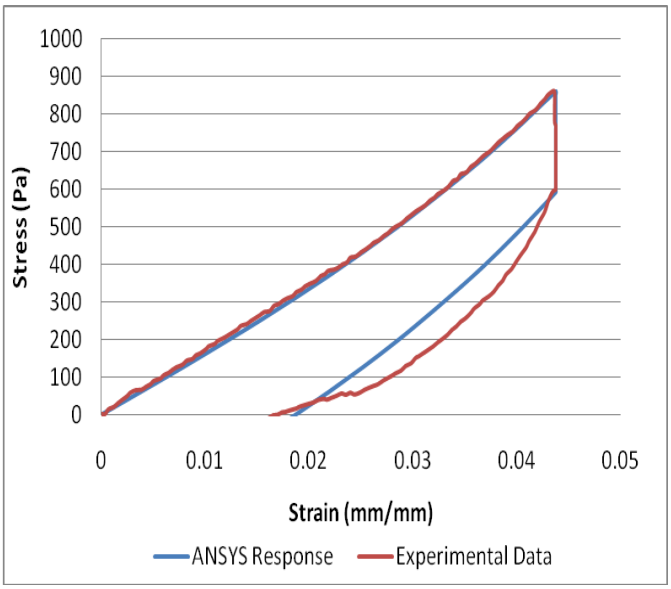

Figure 17: RSA – Stress v. Strain – Stored Human Tissue 4.38% Strain with ANSYS Model

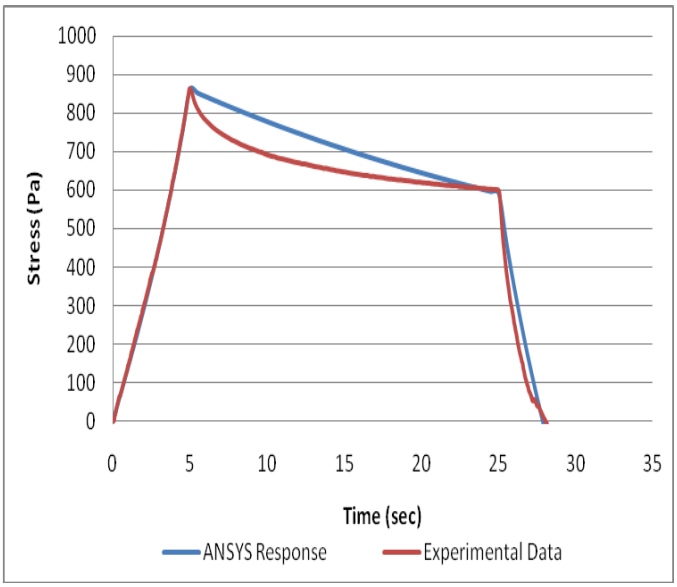

Figure 18: RSA – Stress v. Time – Stored Human Tissue 4.38% Strain with ANSYS Model

Figures 17 and 18 represent the a slight increase of strain acting on human brain tissue, when compared to Figures 15 and 16. Notice that the compression portion of the Experimental Data from Figure 17 has a concave shape, differing from the lower strain. The concave shape was expected, and resembled the stress v. strain curves produced by the other mechanisms Instron: Figures 5 and 6, TestResources: Figure 14. The ANSYS response in Figure 17 nearly overlays the Experimental Data. As stated previously, the Stress v. Time graph was generated after the initial analysis of the model representation. When comparing it to the lower strain the hold still had a concave representation, with an initially steap (very negative slope), which then worked its way toward zero. In Figure

18, the initial slope was not nearly as steep when compared to the lower strain, yet the beginning and ending points remained accurate, when comparing the Expereimental Data and the ANSYS Response. Differences between Figures 16 and 18 were present in the compression portion and the reslease of strain portions where the raw data seemed to begin to deviate from a linear response.

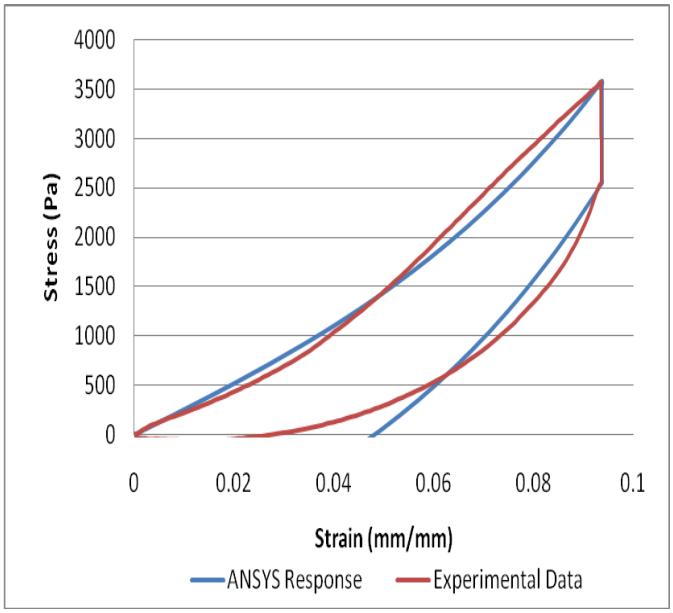

Figure 19: RSA – Stress v. Strain – Stored Human Tissue 9.37% Strain with ANSYS Model

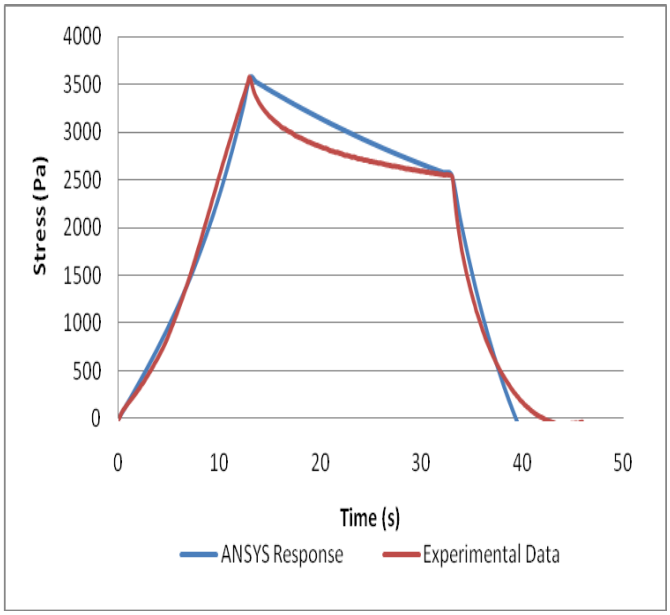

Figure 20: RSA – Stress v. Time – Stored Human Tissue 9.37% Strain with ANSYS Model

Figures 19 and 20 represent the a increase of strain on stored human tissue compared the previous figures. Notice that the compression portion of the Experimental Data from Figure 19 continues to have a concave shape, but it was more concave near the initial application of strain and then becomes very linear for the remainder of the compression. As stated previously, the Stress v. Time graph was generated after the initial analysis of the model representation. When the Experimental Data of the Stress v.

Time graph was compared to the lower strains, the hold portion response remained concave, but the initial slope continued to become less steep, relative to the rest of the curve. Similarly, the ANSYS Response did not accurately depict the hold portion but the end points of the model and the raw data were fairly similar. The compression portion and the release portion deviated even farther from linearity.

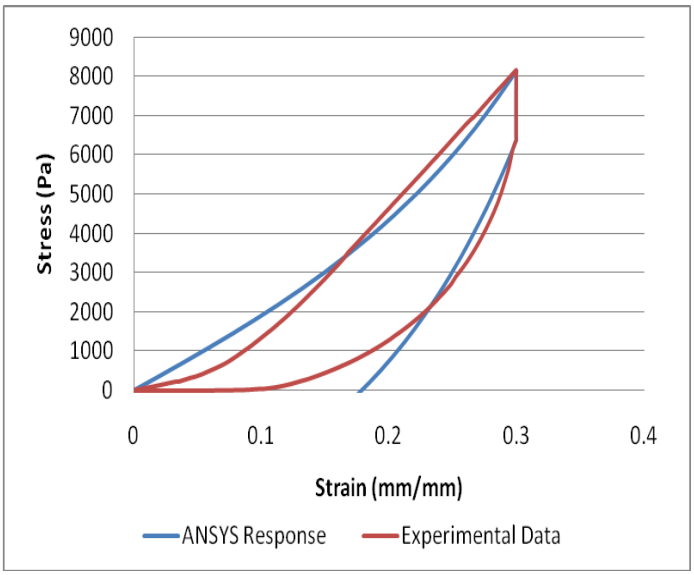

Figure 21: RSA – Stress v. Strain – Stored Human Tissue 29.86% Strain with ANSYS Model

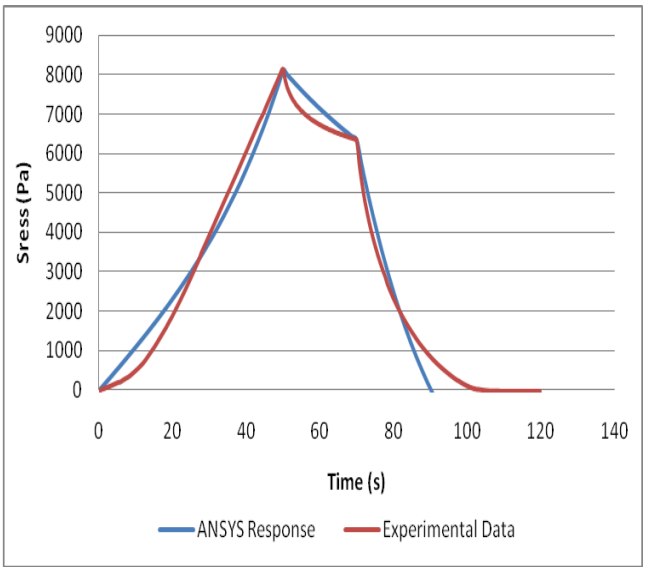

Figure 22: RSA – Stress v. Time – Stored Human Tissue 29.86% Strain with ANSYS Model

Figures 21 and 22 represent the highest strain applied to stored brain tissue. Notice that the compression portion of the Experimental Data from Figure 21 continues to have a concave shape, but the slope was relatively low at the beginning, then increases very quickly around 6% strain. That exact response was difficult to capture, but the ANSYS response seen in Figure 21 provided the lowest average relative error (discussed later). When the Experimental Data of the Stress v. Time graph was compared to the lower strains, the hold portion response remained concave. The ANSYS Response did

not accurately depict the hold portion but the end points of the model and the raw data were fairly similar. The compression portion and the release portion deviated from linearity even farther than all of the previous tests.

Figures 15-22 are ANSYS responses overlayed with the data from Figures 4 and 5, in an attempt to represent the accuracy of the model response of the tissue when a compression test was applied. A hope was that the constants would present a trend that could be used to further predict the reaction of the tissue. Table 2 shows each of the constants for each test.

	Constants					
	Hyper-Elastic		Visco-Elastic			
% Strain	C 10, C 01	C 20, C 02	a1	t1	a2	t2
0.70%	5480	5*	0.49	0.01	0.365	25
4.38%	2600	45000	0.49	0.01	0.365	34
9.37%	4150	30000	0.49	0.01	0.365	37
29.86%	2950	300	0.49	0.01	0.365	47

Table 2: Table of Final Constants

*** = Any number could be placed in there because at low strains C20,C02 only contributes to how concave the application reaction is**

The strain rates were supposed to be strains 1%, 5%, 10% and 30%, but each of them differed from the actual tests performed. This not due to the machine used, the RSA, but instead to an inaccurate height used to calculate the tests conducted. This issue was easily corrected by placing the sample in the RSA before inputing the displacements, and using the RSA to accurately measure the height.

There were few possible trends that could be recognized that could be useful from Table 2. For low strains C_{20},C_{02} barely affected the concavity of the model during the application of strain, but as the max strain increases, it has a variety of effects on the overall model, none of which can be definitely depicted. This created issues for accuracy at high strains. One trend seen specifically in the Viscoelastic Constant was that each remained constant except t2. Specifically in the human stored samples, t2 increases consistently, which with further research could be analyzed better.

Once the stored human brain tissue was tested, it was important to examine similar tests conducted on fresh tissue for the Macaque Monkeys. The only test that provided a comparable set of data, was the data from Figure 11, which had a strain of 8%. Figure 18, the data from Figure 12 with a model overlaying it, was also included because it was hoped to examine the changes in the constants due to high strains and strain rates.

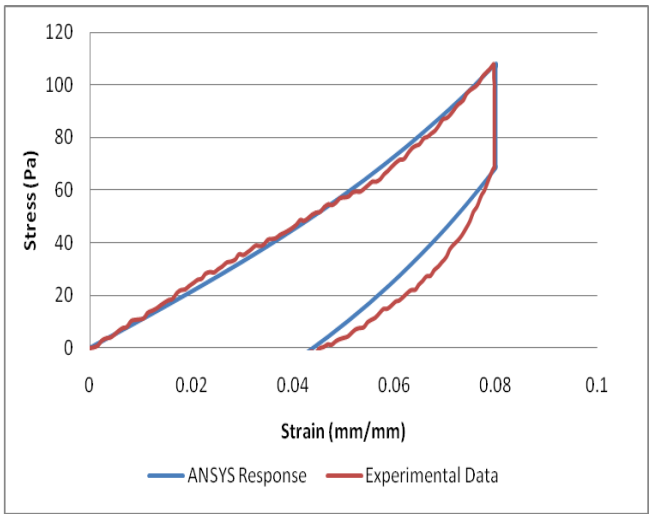

Figure 23: RSA – Stress v. Strain – Fresh Monkey Tissue 7.9% Strain at a Strain Rate of 5 mm/min with ANSYS Model

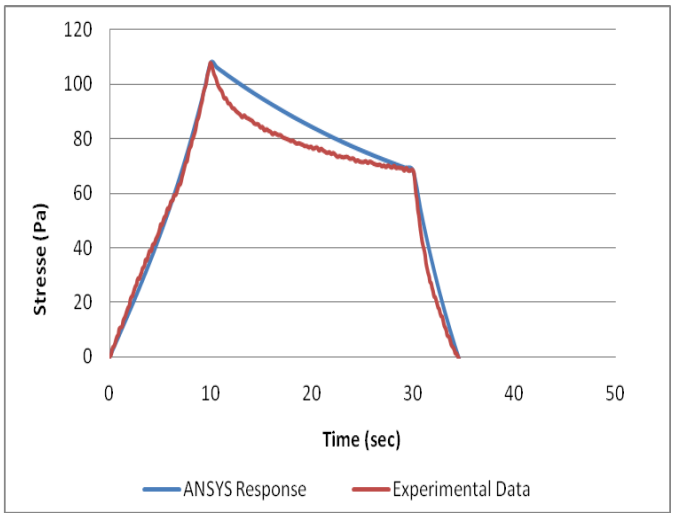

Figure 24: RSA – Stress v. Time – Fresh Monkey Tissue 7.9% Strain at a Strain Rate of 5 mm/min with ANSYS Model

Figures 23 and 24 represent the lowest strain applied to the fresh brain tissue samples. Notice that the compression portion of the Experimental Data from Figure 23 has a concave shape similar to other tests performed. The beginning and ending points of the Stress v. Strain curves are nearly identical between the ANSYS Response and the Experimental Data. After performing the iterations in order to generate the Stress v. Strain curves, it was determined that the Stress v. Time curve would provide a better representation of the viscoelastic performance, as seen in Figure 24. During the compression and release-of-strain portion the ANSYS Response and the Experimental Data are very comparable, with similar beginning and ending points. The issue was that the model does not accurately depict the response during the hold.

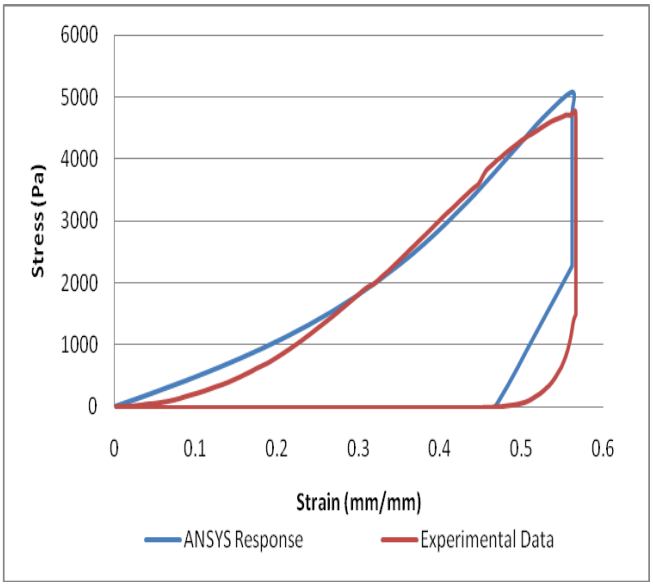

Figure 25: RSA – Stress v. Strain – Fresh Monkey Tissue 56.7% Strain at a Strain Rate of 40 mm/min with ANSYS Model

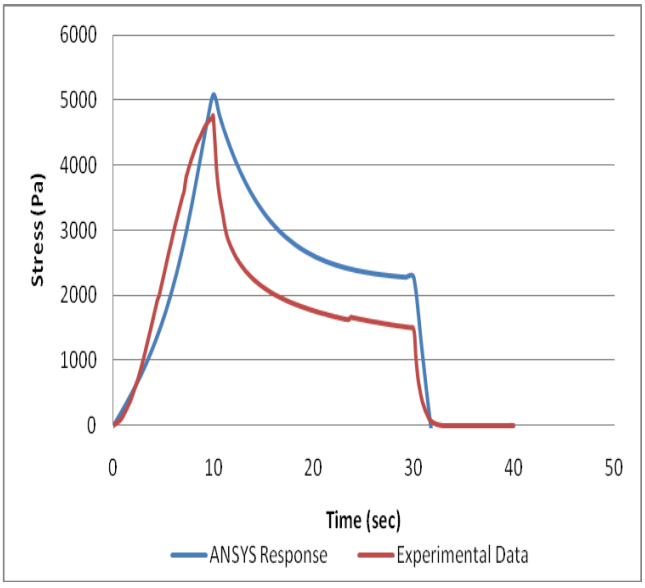

Figure 26: RSA – Stress v. Strain – Fresh Monkey Tissue 56.7% Strain at a Strain Rate of 40 mm/min with ANSYS Model

Figures 25 and 26 represent a very different test when compared to the other test performed on fresh tissue, because the strain and strain rate were both made considerably higher. Notice that the compression portion of the Experimental Data from Figure 25 has a concave and convex shape. During the beginning of the strain the response in cocave and moves towards a center portion which was seemingly linear, followed by a convex portion, which was most likely due to the test mechanism slowing down to a stop. The response developed in ANSYS was un able to mimic this presponse. The beginning and ending points of the Stress v. Strain curves are not really near oneanother when comparing the ANSYS Response and the Experimental Data, unlike the lower strain/strain rate test performed. When examining the Stress v. Strain graph, the compression and release-of-strain portions of the ANSYS Response and the Experimental Data, have different beginning and ending points. When specifically examining the hold portion of the test the general shape and overall disipation of stress over that time was accurately depicted by the model.

The constants for Figures 23 and 25 can be seen in Table 3. One problem was that C20,C02 was a negative number for the high strain/high strain rate test which was not desired. The negative number was a red flag that makes it obvious that the hyperelastic/viscoelastic model from ANSYS are not sufficient for tests conducted at high strain rates and high strains.

	Constants					
	Hyper-Elastic		Visco-Elastic			
% Strain	C 10, C 01	C 20, C 02	a1	t1	a2	t2
8.00%	173	1050	0.49	0.01	0.365	26
56.70%	750	-50	0.49	0.01	0.365	5

Table 3: Constants for Fresh Monkey Tissue

When comparing the trends seen in Table 3 to that of the trends in Table 2 there was one difference that stands out, and that centers around the t2 constant. The trend from the stored tissue was that as the strain increases t2 increases, which does not seem to apply to Table 3 therefore does not apply to fresh monkey tissue. This does not necessarily refute the possible trend because as discussed before, the model used to model the high strain/high strain rate was not sufficient; therefore the constants are not appropriate.

With this collection of ANSYS models, it was important to examine the accuracy between the models and the raw data before examining the constants for trends. In order to examine the data it was chosen to use average relative error between the data points of the model and the raw data, as seen in Equation (3). The way the model was set up and responded we specifically wanted to examine the accuracy of the compression portion of the test as well as the hold.

$$\text{Average Relative Error} = \frac{\sum_{n=1}^{i} \frac{Theoretical_i - Experimental_i}{Theoretical_i}}{i} \quad \textbf{(3)}$$

Because the model and raw data points of the compression response do not have points that correspond exactly, a series of interpolations and averages were applied when need-be to provide sufficient data for comparison. The average relative error can be seen in Table 4.

Another portion of interest within the data was the dissipation of stress during holding period. If this relaxation portion of the data could be captured in the model, it could help to understand the viscoelastic reaction. The analysis examined in this paper centered around the two end points of the hold period, because the relaxation was not accurately captured by the models. To analyze the error of the relaxation/holding period, a relative error was calculated and can be seen in Table 4. The individual relative error data that was averaged in order to examine the compression portion of the test can be found in Appendix B.

			Average Relative Error	Relative Error
	Strain Rate (mm/min)	Strain (mm/mm)	Compression	Relaxation/Hold
HUMAN	5	0.007	13.12%	1.92%
	5	0.044	2.32%	4.54%
	5	0.094	7.06%	3.24%
	5	0.299	21.76%	0.21%
MONKEY	5	0.080	5.59%	0.84%
	40	0.566	22.88%	16.27%

Table 4: Average Relative Error

Overall between the compression and holding portions of the test, the overall accuracy of the models was fairly good. The models of the strains between 4% and 10% of both the human stored tissue and the macaque fresh tissue produced the most accurate models, which was encouraging because that was the strains of most interest.

V. Future Work and Conclusion

The purpose of this research was to examine of the stress-strain behavior of stored and fresh brain tissue. The main objective was to derive any possible correlations between the stored and fresh tissue. In the end there were few correlations able to be drawn between fresh and stored tissue as seen in Table 6, which compares the constants from the modeling of both fresh and stored tissue with strains approximately 8-10%, compared with Dr. Miller's constants from Miller [4].

		Constants					
		Hyper-Elastic		Visco-Elastic			
	% Strain	C 10, C 01	C 20, C 02	a1	t1	a2	t2
Stored Tissue	**9.37%**	4150	30000	0.49	0.01	0.365	37
Fresh Tissue	**8.00%**	173	1050	0.49	0.01	0.365	26
Dr. Miller's Fresh	**ALL Strains**	263	491	0.45	0.5	0.365	50

Table 5: Constants for Similar Test Parameters and Varied tissues

The fresh tissue compares favorably to Dr. Miller's constants, rather than the stored tissue. That was expected, because his constants were derived from fresh tissue samples, but only examined at low strains. With further research, expanding the number

of tests there could possibly be a correlation drawn when the strain rates are held constant and the strains are changed. With this examination into macro-strain, there could possibly the same breakthrough into micro-strain opening doors for further research into neurological implants.

There still remains opportunity in this field. This research did not necessarily prove any correlation, but it did not disprove that they exist either, which was the most important part. The groundwork has been laid for future work to possibly find correlations making it unnecessary to need fresh tissue to conduct material property tests.

The initial work should center around conducting more tests at a single strain rate and strain, in order to attempt to verify data, and provide a greater test sample from which to compare. Also, gaining more fresh tissue and determining the best test setup to use. It was noticeable that as the size of the load cell directly impacted the accuracy of the tests. The larger load cells that were present in the Instron (50kN and 500N load cells) were unable to capture fresh tissue data where the smaller load cells present in the TestResources Mechanism (10N load cell) and the RSA (20N load cell) collected more accurate data. The fact that the TestResources Mechanism has the smallest load cell increases the desire to conduct additional tests using it.

In the end the research did not draw and definite conclusions but was able set up future work to succeed and begin testing with a solid set of prior knowledge.

Bibliography

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[2] R.A. Green, N.H. Lovell, G.G. Wallace, L.A. Poole-Warren, "Conducting Polymers for Neural Interfaces: Challenges in Developing an Effective Long-term Implant", *Biomaterials*, 2008, Vol. 29, pp 3393-3399.

[3] K. Miller and K. Chinzei, "Modelling of Brain Tissue Mechanical Properties. Bi-phasic versus Single-phase Approach," in Proc. 3rd Intl Symp Comput Methods in Biomech & Biomed Eng, 1997.

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Appendix A:

Original height (mm)	9.5									
Original Diameter (mm)	30									
Block duration (sec)	2.814282		Division Factor	26						
Distance Compressed (mm)	4.5									
Final strain (mm/mm)	-0.65385									
Final true strain (mm/mm)	-0.64185									
True strain rate (mm/mm/s)	-0.00877	1.0/min								
Block Time (secs)		Block Start Time (s)	Block #	True strain rate (mm/mm/s)	Change in height (mm)	Actual height (mm)	Compressive extension rate (mm/s)	Serial No.		
2.814282368		0	1	-0.00877193	0	9.5	-0.083333335	1		-0.00877193
		2.814282368	2	-0.00877193	-0.234523535	9.265476465	-0.081276111	2		-0.00877193
		5.62856473 5	3	-0.00877193	-0.228733926	9.036742539	-0.079269673	3		-0.00877193
		8.442847103	4	-0.00877193	-0.223087243	8.813655296	-0.077312767	4		-0.00877193
		11.25712947	5	-0.00877193	-0.217579958	8.596075338	-0.075404171	5		-0.00877193
		14.07141184	6	-0.00877193	-0.212208629	8.383866709	-0.073542692	6		-0.00877193
		16.88569421	7	-0.00877193	-0.206969901	8.176896808	-0.071727166	7		-0.00877193
		19.69997657	8	-0.00877193	-0.2018605	7.975036308	-0.06995646	8		-0.00877193
		22.51425894	9	-0.00877193	-0.196877233	7.778159075	-0.068229467	9		-0.00877193
		25.32854131	10	-0.00877193	-0.192016986	7.58614209	-0.066545107	10		-0.00877193
		28.14282368	11	-0.00877193	-0.187276722	7.398865367	-0.064902329	11		-0.00877193
		30.95710604	12	-0.00877193	-0.18265348	7.216211887	-0.063300106	12		-0.00877193
		33.77138841	13	-0.00877193	-0.178144371	7.038067516	-0.061737436	13		-0.00877193
		36.58567078	14	-0.00877193	-0.173746576	6.86432094	-0.060213343	14		-0.00877193
		39.39995315	15	-0.00877193	-0.169457349	6.694863591	-0.058726875	15		-0.00877193
		42.21423552	16	-0.00877193	-0.165274008	6.529589582	-0.057277103	16		-0.00877193
		45.02851788	17	-0.00877193	-0.16119394	6.368395642	-0.055863121	17		-0.00877193
		47.84280025	18	-0.00877193	-0.157214596	6.211181046	-0.054484045	18		-0.00877193
		50.65708262	19	-0.00877193	-0.153333488	6.057847558	-0.053139015	19		-0.00877193
		53.47136499	20	-0.00877193	-0.149548192	5.908299366	-0.051827188	20		-0.00877193
		56.28564735	21	-0.00877193	-0.145856343	5.762443023	-0.050547747	21		-0.00877193
		59.09992972	22	-0.00877193	-0.142255633	5.620187391	-0.04929989	22		-0.00877193
		61.91421209	23	-0.00877193	-0.138743812	5.481443578	-0.048082839	23		-0.00877193
		64.72849446	24	-0.00877193	-0.135318687	5.346124891	-0.046895833	24		-0.00877193
		67.54277682	25	-0.00877193	-0.131978117	5.214146775	-0.045738131	25		-0.00877193
		70.35705919	26	-0.00877193	-0.128720014	5.08542676	-0.044609008	26		-0.00877193
120	hold	73.17134156	27	0	0		0	27		
84	unloading	204	28				-0.060331998	28		

Appendix B:

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.0000	0.00	0.00	0.00%
0.0007	24.71	22.33	10.68%
0.0013	55.44	44.50	24.59%
0.0023	92.28	77.59	18.93%
0.0036	154.32	121.80	26.71%
0.0050	192.18	165.95	15.81%
0.0063	226.00	210.03	7.61%
0.0073	241.56	243.06	0.62%
			13.12%

Figure 1: Relative Error for Given Strains During Compression of Stored Tissue to a Strain of 0.7% at a Strain Rate of 5 mm/min

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.0000	0.00	0.00	0.00%
0.0043	73.83	70.14	5.27%
0.0087	147.98	141.32	4.71%
0.0152	264.29	252.01	4.87%
0.0219	380.86	370.21	2.88%
0.0284	501.93	499.23	0.54%
0.0351	648.44	642.56	0.92%
0.0395	755.71	747.88	1.05%
0.0436	856.35	862.34	0.69%
			2.32%

Figure 2: Relative Error for Given Strains During Compression of Stored Tissue to a Strain of 4.4% at a Strain Rate of 5 mm/min

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.0000	0.00	0.00	0.00%
0.0036	91.58	91.58	0.01%
0.0071	163.08	183.60	11.18%
0.0127	271.08	323.20	16.13%
0.0200	430.64	514.09	16.23%
0.0270	605.57	713.17	15.09%
0.0343	819.57	923.55	11.26%
0.0413	1082.63	1148.52	5.74%
0.0486	1382.73	1391.59	0.64%
0.0559	1723.20	1656.48	4.03%
0.0633	2098.37	1947.12	7.77%
0.0709	2481.63	2267.71	9.43%
0.0774	2806.06	2622.72	6.99%
0.0849	3166.91	3016.93	4.97%
0.0892	3363.48	3285.50	2.37%
0.0935	3534.82	3572.67	1.06%
			7.06%

Figure 3: Relative Error for Given Strains During Compression of Stored Tissue to a Strain of 9.37% at a Strain Rate of 5 mm/min

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.0000	0.00	0.00	0.00%
0.0118	67.51	216.27	68.79%
0.0238	148.50	434.30	65.81%
0.0418	282.16	765.95	63.16%
0.0598	492.68	1105.22	55.42%
0.0777	798.98	1454.54	45.07%
0.0956	1218.98	1816.58	32.90%
0.1137	1697.65	2194.27	22.63%
0.1316	2237.20	2590.88	13.65%
0.1496	2830.20	3010.10	5.98%
0.1676	3482.88	3456.08	0.78%
0.1855	4121.18	3933.56	4.77%
0.2035	4754.94	4448.00	6.90%
0.2215	5380.97	5005.68	7.50%
0.2394	6016.87	5613.92	7.18%
0.2574	6667.24	6281.31	6.14%
0.2754	7285.17	7017.92	3.81%
0.2965	8043.86	7835.74	2.66%
0.2995	8150.30	8128.99	0.26%
			21.76%

Figure 4: Relative Error for Given Strains During Compression of Stored Tissue to a Strain of 29.86% at a Strain Rate of 5 mm/min

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.0000	0.00	0.00	0.00%
0.0040	4.34	4.23	2.44%
0.0080	9.56	8.48	12.81%
0.0141	16.49	14.89	10.72%
0.0221	26.96	23.64	14.05%
0.0302	35.84	32.74	9.48%
0.0381	43.73	42.34	3.28%
0.0460	53.14	52.62	0.99%
0.0540	60.57	63.73	4.96%
0.0619	72.53	75.87	4.41%
0.0702	87.66	89.23	1.76%
0.0750	98.08	98.29	0.22%
0.0797	99.85	107.97	7.52%
			5.59%

Figure 5: Relative Error for Given Strains During Compression of Fresh Tissue to a Strain of 8% at a Strain Rate of 5 mm/min

Approximate Strain	Stress Raw Data	Stress Model Response	Difference
0.000	0.00	0.00	0.00%
0.028	26.02	131.07	80.15%
0.056	74.62	265.22	71.87%
0.098	214.68	475.32	54.84%
0.155	493.71	780.33	36.73%
0.210	898.38	1127.95	20.35%
0.265	1438.69	1535.88	6.33%
0.324	2055.52	2025.22	1.50%
0.379	2739.13	2619.08	4.58%
0.435	3457.02	3335.01	3.66%
0.491	4211.06	4157.17	1.30%
0.526	4521.04	4674.31	3.28%
0.567	4429.26	5081.35	12.83%
			22.88%

Figure 5: Relative Error for Given Strains During Compression of Fresh Tissue to a Strain of 56.6% at a Strain Rate of 40 mm/min